Protein sorting to intracellular compartments

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The organization of eukaryotic cells depends on correct targeting of proteins and lipids to the organelles at which they function, but how organelle identity is maintained in the face of a constant flux of material is a major problem for the cell. New mechanisms addressing this question were revealed at the Minisymposium on "Membrane Traffic: Dynamic and Regulation."

Starting with the endoplasmic reticulum (ER), **Silvere Pagant** (Miller lab) showed that some plasma membrane (PM) proteins require multiple signals to drive capture into COPII vesicles. One signal comes from the cargo protein itself, and the second comes signal from a cargo receptor; both signals simultaneously engage the cargo adaptor for the COPII coat, Sec24. **Prasanna Satpute-Krishnan** (Lippincott-Schwartz and Hegde labs), recipient of the 2014 Merton Bernfield Award, presented her work on a novel quality-control mechanism for glycosylphosphatidylinositol (GPI)-anchored proteins called RESET (for rapid ER stress-induced export). ER stress causes receptor-mediated exit of GPI-anchored proteins from the ER through the secretory pathway to the PM, from which they are endocytosed and degraded in lysosomes. Only misfolded GPI-anchored proteins bind tightly to the cargo receptor, Tmp21, providing a new paradigm in ER stress clearance. Moving from the ER to the Golgi, **Mie Wong** (Munro lab) presented an elegant system to test the function of a family of diverse Golgi-localized coiled-coil proteins. When different golgins were ectopically attached to mitochondria, specific classes of vesicles were redirected to mitochondria, clearly demonstrating a vesicle capture role for these proteins.

A possible mechanism of lipid transfer from the ER to the PM was revealed by a structural study presented by **Chris Schauder** (Reinisch and de Camilli groups). The synaptotagmin-like mitochondrial-lipid binding protein (SMP) domain of the ER–PM tether E-Syt2 forms a long hydrophobic channel that can harbor multiple phospholipid molecules. Two SMP domains form a stacked dimer to double the length of the channel. Continuing the theme of lipid composition in organelle identity, **Cathy Jackson** presented her group's results showing how amphipathic helices (AHs) of distinct chemistries specifically target different organelles through recognition of organelle lipid composition. Regulation of a lipid-binding AH of the Arf guanine nucleotide exchange factor (GEF) GBF1 mediates its localization to either the Golgi or lipid droplets. Looking at a related Arf GEF, yeast Sec7, **Brian Richardson** (Fromme lab) reported the first crystal structure of a noncatalytic region of these proteins. The N-terminal region is made up of α-helices forming a series of armadillo folds that form an extended platform. This structure provides insight into how this region is involved in dimerization and protein interactions.

New vesicle tethering and targeting mechanisms were reported, with **Chris Stroupe** presenting how the homotypic fusion and protein sorting (HOPS)/class C Vps tethering complex connects specific membrane compartments. This complex binds to a Rab GTPase in one membrane and directly to a second, highly curved membrane through a curvature-sensing amphipathic lipid packing sensor (ALPS) motif. **Margaret Heider** (Munson lab) provided the most comprehensive view to date of the architecture of the exocyst complex, a multisubunit tether that targets secretory vesicles to the PM. The session ended with a talk by **Christine Insinna-Kettenhofen** (Westlake group) reporting on a new mechanism for targeting of vesicles to cilia mediated by the epidermal growth factor receptor substrate 15 homology domain–containing (EHD) proteins. These proteins are localized to vesicles, where they cooperate with the Rab8-Rab11 cascade and soluble *N*-ethylmaleimide–sensitive factor attachment protein receptors (SNAREs) to regulate morphological changes to the vesicle membrane important for fusion.

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